Remarks

Claims 41-51 are pending in this application. Claim 42 is amended to remove the recitation of (S)-didesmethylsibutramine and (R,S)-didesmethylsibutramine, which are added as new dependent claims 50 and 51, respectively. Claim 49 is amended to remove the recitation of certain second active agents. No new matter has been added.

Applicants respectfully submit that the pending claims are allowable for at least the following reasons.

A. The Objection of the Abstract Should Be withdrawn

On page 2 of the Office Action, the abstract of the current specification is objected to because "the first paragraph should recite the compound(s) ... that are to be administered in the claimed methods." (Office Action, page 2). As suggested, the abstract is amended to recite such compounds, and a replacement abstract page is provided herein. In view of these amendments, Applicants respectfully request that the objection of the abstract be withdrawn.

B. The Rejection Under 35 U.S.C. § 112 Should Be Withdrawn

On pages 2-5 of the Office Action, claim 49 is rejected as allegedly containing subject matter not described in the specification. In particular, it is alleged that no description of "a drug for treating or preventing depression that is an antimonic agent, a cardiovascular agent, an antiviral agent, an antibiotic, an antifungal or an antineoplastic" is provided in the specification "with sufficient clarity." Although Applicants respectfully disagree,[1] claim 49 is amended to remove the recitation of these agents solely to expedite the prosecution of the present application. In view of these amendments, Applicants respectfully request that the rejection of claim 49 under 35 U.S.C. § 112 be withdrawn.

[1] This is because all of those agents are expressly provided in the specification, and those terms are wekk-known and understood by one of ordinary skill in the art. Thus, such a person would have had no reason to believe that the inventors were not in possession of the claimed method.

C. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 5-6 of the Office Action, claims 41-49 are rejected as allegedly obvious over Scott *et al.*, *Br. J. Pharmacol.*, 111: 97-102 (1994) ("Scott") in view of Jeffery *et al.*, *J. Chem. Soc., Perkin Trans.*, 1: 2583-9 (1996) ("Jeffery") or Jacques *et al.*, *Enantiomers, Racemates, and Resolutions*, Wiley-Intersciences (1981) ("Jacques"). In particular, the Examiner alleges that the claims are obvious based on her assertion that: 1) Scott "teaches a method of treating depression comprising administering didesmethylsibutramine"; and 2) "either Jeffery or Jacques teaches means of obtaining optically pure enantiomers of the metabolites of sibutramine." (Office Action, page 6). Applicants respectfully traverse this rejection.

Under current law, a prior art reference or references cannot render a claim obvious unless the PTO provides evidence that the reference or references meet a three-part test for *prima facie* obvious. To begin with, the prior art reference or references must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." *See In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316-17. Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002). Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2 d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, "[b]oth the suggestion and the reasonable expectation of success 'must be founded in the prior art, not in the applicant 's disclosure.'" *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at 1515-16 (quoting *In re Vaeck* , 947 F.2d 488, 493, 20

U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996). These criteria must be satisfied with factual and objective evidence found in the prior art; an examiner's conclusory statements cannot form a basis for a *prima facie* case of obviousness. *See In re Sang-Su Lee* , 277 F.3d 1338, 1343-44 (Fed. Cir. 2002).

Applicants respectfully submit that no *prima facie* case of obviousness is established for claim 41 by Scott.[2] This is because, contrary to what the Examiner appears to suggest, Scott does not disclose or suggest "a method of treating depression comprising administering didesmethylsibutramine." (Office Action, page 5). All Scott discloses is that didesmethylsibutramine has "a similar pharmacological profile to the parent compound *in vivo*, but are up to 100 fold more potent than sibutramine ... *in vitro*." (Scott, Introduction) (emphasis added). No where in Scott it is disclosed or suggested that didesmethylsibutramine is administered to a patient to treat or prevent depression.

Furthermore, Scott, by disclosing that didesmethylsibutramine has a pharmacological profile similar to the parent compound *in vivo*, would not have provided those of ordinary skill in the art with any motivation to administer didesmethylsibutramine to a patient.[3] In view of this absence of any suggestion or motivation for the administration of didesmethylsibutramine to a patient, much less administration to a patient for the treatment or prevention of depression, Applicants respectfully submit that claim 41 is not obvious over Scott.

Further, Applicants point out that the combination of Scott and Jeffery or Jacques also fails to establish that the claims reciting enantiomers of didesmethylsibutramine (now claims 42 and 50) are *prima facie* obvious. First, the combination of Scott and Jeffery/Jacques fails to teach or suggest enantiomers of

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[2] Jeffery or Jacques is provided to show that "means of obtaining optically pure enantiomers" are disclosed (Office Action, page 6), and thus, is irrelevant to the rejection of claim 41 which does not recite enantiomers.

[3] Although didesmethylsibutramine is reportedly more potent than the parent compound *in vitro*, it is clear that *in vivo* activity is what matters when determining an agent should be "administered to a patient."

didesmethylsibutramine, much less administration of such enantiomers to a patient for the treatment of depression. As the Examiner recognizes, there is no question that Scott does not disclose or suggest enantiomers of didesmethylsibutramine. Further, contrary to what the Examiner appears to believe, Applicants respectfully point out that Jeffery does not disclose or suggest enantiomers of didesmethylsibutramine. This is because compound 5a in Jeffery, although showing cis/trans isomerism, does not show stereoisomerism. In addition, Jacques is a text book directed generally to the stereoisomerism and resolution of stereoisomers, and thus, does not specifically disclose enantiomers of didesmethylsibutramine. Therefore, the combination of Scott and Jeffery/Jacques indeed fails to disclose or suggest the enantiomers recited by claims 42 and 50. For this reason alone, Applicants respectfully submit that the rejection of the claims should be withdrawn.

More important, however, is the fact that the combination of references does not provide any motivation for those of ordinary skill in the art to arrive at the claimed method. In this regard, the Examiner alleges that the use of the enantiomers is obvious because "either Jeffery or Jacques teaches means of obtaining optically pure enantiomers." (Office Action, page 6). However, as well-settled, "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggest the desirability of the combination." (*Manual of Patent Examining Procedure*, § 2143.10, citing *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990)). Clearly, no such suggestion of desirability of using the enantiomers is present in Scott, Jeffery, or Jacques.

Despite this fact, the Examiner, without providing any specific evidence, alleges that the use of enantiomers are obvious because "such isomers often exhibit a lower side effect profile or an unexpected beneficial property." (Office Action, pages 5-6). By this allegation, the Examiner is essentially asserting that the use of stereoisomers are *per se* obvious over the disclosure of their racemic mixture. However, Applicants respectfully point out that such an allegation is flatly contrary to the well-established legal principles concerning the obviousness of structurally similar compounds.

This is because each obviousness determination should rest on its own facts. (*See, e.g., In re Grabiak*, 769 F.2d 729, 731 (Fed. Cir. 1985) ("Generalization should be avoided insofar as specific chemical structures are alleged to be prima facie

obvious one from another.")). Thus, *prima facie* obviousness of a claimed compound cannot be established if its assertion is based on nothing more than a structural similarity between the claimed compound and those in the prior art. (*See, e.g., Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000) ("a prima facie case of obviousness requires structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions .") (emphasis added)).

Accordingly, the question is whether those of ordinary skill in the art would have been motivated to make and use the claimed invention, not whether such persons could have made the claimed invention. (*See In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990) (holding that the mere fact that prior art references can be combined or modified does not render the combination obvious unless the prior art also suggests the desirability of the combination)). As discussed above, neither Jeffery nor Jacques suggests the desirability of the claimed invention, and the Examiner does not provide any evidence to the contrary. Without addressing any of these facts, the Examiner simply concludes that the claims are obvious because racemic mixture was disclosed in Scott and its enantiomers could be made based on Jeffery[4] or Jacques. However, such a conclusory statement cannot form a basis for a *prima facie* case of obviousness. (*In re Sang-Su Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002)).

For further support, Applicants submit herewith a copy of *In re Holy*, 2004 WL 77012 (B.P.A.I. 2004), which addressed issues almost identical to those raised in the present application. In *Holy*, claims at issue recited a genus of enantiomerically pure chemical compounds. The claims were rejected under 35 U.S.C. § 103 over, among others, a reference which disclosed a racemic mixture of a compound encompassed by the chemical structure recited by the claims. (*See Holy*, page *3). The examiner in *Holy* rejected the claims as allegedly obvious based merely on case law without providing any references that provide motivation. (*See id.*). In doing so, the examiner in *Holy* provided a reasoning substantially identical to that provided in the present application by the Examiner, *i.e.*, that a stereoisomer is *prima facie* obvious over prior disclosure of its racemic mixture. (*See id.*).

In reversing the examiner's rejection, the Board stated that:

[4] Again, Jeffery does not even disclose the enantiomers of didesmethylsibutramine, much less treating or preventing depression using the enantiomers.

> [i]n order to make a prima facie case of obviousness based on the structural similarity, in this case similarity between the claimed optical isomer and its racemate taught by the prior art, not only must the structural similarity exist, but the prior art must also provide reason or motivation to make the claimed compound.

(*Id.* at page *4, citing *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990); *In re Mayne*, 104 F.3d 1339, 1341 (Fed. Cir. 1997); and *In re Payne*, 606 F.2d 303, 313 (C.C.P.A. 1979)) (emphasis added).

The Board went on to hold that the rejection cannot be sustained because the references cited by the examiner in *Holy* did not provide any motivation, and the examiner did not "set forth any facts or findings to support the motivational statement, especially since all that is currently being claimed is a single isomer." (*Id.*, citing *In re Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002)) (emphasis added).

Further, in addressing the examiner's reliance on case law "for the proposition that an optically pure form of a compound is per se obvious over a disclosure of a racemic mixture of the compound," the Board held that such reliance is misplaced because "one cannot rely on case alone ... to provide the motivation to modify a prior art compound." (*Id.* at page *6) (emphasis added). The Board concluded that the question is "whether there is something in the prior art as a whole to suggest the desirability... of making the combination," and reversed the examiner's rejection because no such desirability was shown by the cited references. (*Id.*).

As can be seen, the facts and holdings of *Holy* are directly applicable to the present application. As in *Holy*, the Examiner's rejection is based solely on the allegation that a stereoisomer is *prima facie* obvious over the prior disclosure of its racemate. As in *Holy*, there is no disclosure regarding the desirability of using the enantiomers of didesmethylsibutramine in the references cited by the Examiner. Therefore, Applicants respectfully submit that the rejection of the claims 35 U.S.C. § 103 cannot be sustained, and thus request that this rejection be withdrawn.

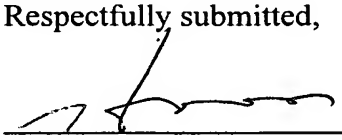
Conclusion

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that the rejection of the claims be withdrawn.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

Date May 25, 2006



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2004 WL 77012 (Bd.Pat.App & Interf.)
(Cite as: 2004 WL 77012 (Bd.Pat.App & Interf.))

*1 THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)

EX PARTE ANTONIN HOLY, HANA DVORAKOVA, ERIK D. A. DE CLERCQ, JAN M. R. **BALZARINI**

Appeal No. 2000-1024
Application No. 08/379,551

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

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Before WINTERS, GRIMES, and GREEN

Administrative Patent Judges

GREEN

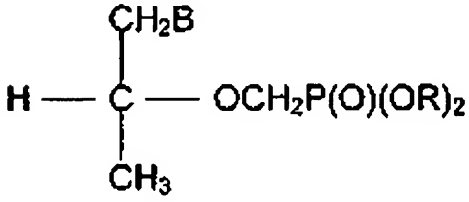
Administrative Patent Judge

ON BRIEF

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 4, 6, 8, 12-19, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94. [FN1] Claim 1 is representative of the subject matter on appeal, and reads as follows:

1. A compound of the formula:



(IA) including salts of such compounds, wherein said compound of Formula IA is substantially free of its enantiomer and wherein B is (a) an unsubstituted purine moiety, (b) a substituted purine moiety substituted independently at the 2 and/or 6 and/or 8 position by amino, halogen, hydroxy, alkoxy, alkylamino, dialkylamino, aralkylamino, pyrrolidino, morpholino, piperidino, benzoylamino, azido, mercapto or alkylthio, or (c) the 8-aza analog thereof, and wherein

B is other than a guanine or 2-amino-6-halopurine;

R is H; and aryl in aralkylamino is a 6-10C aromatic group.

Claims 4, 6, 8, 70, 72, 73, 75, 85, 91, 93 and 94 further limit the compound of claim 1. Claims 12-19 are drawn to a method of preparing the compound of claim 1. Claims 45 through 48, 55, 63 and 65 are drawn to specific compounds that fall within the compound of claim 1.

The examiner relies upon the following references:

Hol [sic] et al. (Holy (US))	4,808,716	Feb. 28, 1989
Alexander et al. (Alexander)	5,130,427	Jul. 14, 1992
Yu et al. (Yu (US))	5,302,585	Apr. 12, 1994
Vemishetti et al. (Vemishetti)	5,476,938	Dec. 19, 1995
Webb, II et al. (Webb (US))	5,650,510	Jul. 22, 1997
European Patent Applications		
Holy et al. (Holy (EP))	0 253 412	Jul. 18, 1986
Webb, II (Webb (EP))	0 269 847	Jun. 08, 1988
Yu et al. (Yu (EP))	0 452 935	Oct. 23, 1991
Starrett et al. (Starrett)	0 481 214	Apr. 22, 1992

*2 Karrer, Organic Chemistry, 2nd English Edition, pp. 92-102 (1946)

The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals, 11th Edition, Article No. 7868, p. 1247 (1989)

In addition, appellants rely upon the following references:

DeClercq et al. (DeClercq), "Antiviral activity of phosphonylmethoxyalkyl derivatives of purine and pyrimidines," Antiviral Research, Vol. 8, pp. 261- 272 (1987)

Holy et al. (Holy (1989)), "Phosphonylmethyl Ethers of Nucleosides and Their Acyclic Analogues," ACS Symposium Series, Vol. 401, pp. 51-71 (1989)

Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holy (US), Webb (EP or US), Yu (US or EP), Starrett, Holy (EP) and Karrer. Claims 12-19 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holy (US), Holy (EP), Webb (EP or US), Vemishetti, Alexander, Yu (US or EP) and the Merck Index. Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 stand rejected under the judicially created doctrine of obviousness-type double patenting over the claims of Holy (US), U.S. Patent No. 4,808,716 (the 'F716 patent) as combined with Yu (EP or US), Holy (EP), Starrett and Karrer. Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 72, 73, 75, 85, 91, 93 and 94 stand rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 5,650,510 (the '510 patent) as combined with Yu (EP or US), Holy (EP), Starrett and Karrer. Finally, claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of copending Application No. 07/925,610. After careful review of the record and consideration of the issues before us, we reverse all of the rejections of record except the provisional obviousness-type

double-patenting rejection of claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 over copending Application No. 07/925,610.

DISCUSSION

Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer. In addition, the obviousness-type double patenting rejections over the '716 patent and the '510 patent as combined with Yu (EP or US), Holy (EP), Starrett and Karrer are included in the analysis of the rejection over the combination of Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer as the rejections state that the claims of the patents are "obvious variant[s] of that claimed herein as discussed in the above 103 rejection." Examiner's Answer, page 7. In addition, appellants rely on the patentability of the end product to overcome the rejection of claims 12-19 over the combination of Holy (US), Holy (EP), Webb (EP or US), Vemishetti (US), Alexander (US), Yu (US or EP) and the Merck Index. Thus, that rejection is also encompassed by the following analysis.

*3 Holy (US) is cited by the rejection for teaching a racemic mixture of 2-phosphonomethoxypropyladenine (PMPA). PMPA is included in the range of structures of claim 1. The rejection also references compound 2 in Table 1, as well as a discussion of the applications of the disclosed compounds, such as anti-viral activity, in column 4, lines 14-19 of the Holy (US) patent. The rejection reasons that:

While the corresponding optical isomer is not particularly disclosed, the claimed R-isomer is held as an obvious variant in view of its very close structural similarity and the fact that one skilled in the art would recognize the existence of such isomers and expect one of a pair to perform better over the other. There is case law regarding the standards of patentability of optical isomers over the corresponding racemic mixture which is on point. See for example, In re Adamson, 125 USPQ 233; Eli Lilly vs. Generix, 174 USPQ 65 regarding the standards of patentability of optical isomers over the corresponding racemic mixture. Note Karrer, cited in Adamson, and applied herein is evidence that it is very well known considerably prior to applicants' effective filing to consider the separation of biologically active racemates in order to determine if one is largely responsible for the desired activity.
Examiner's Answer, page 5.

Webb (EP or US) is apparently cited for teaching derivatives of the compounds as taught by Holy (US). According to the rejection, "Webb does not embrace adenine compound of US Holy but does embrace substituted derivatives thereof having the same sidechain." Examiner's Answer, page 5. Yu (EP or US) is cited for its disclosure of resolution of one of the racemates disclosed by Webb "for elucidation of its antiviral properties," and teaches that the R isomer is "especially effective for treating HIV." Id. at 6.

Holy (EP) was cited for teaching compounds similar to the claimed compounds substituted with different groups, which also have anti-viral activity. Starrett was similarly cited for teaching "that for analogous phosphonate derivatives as claimed herein, substitution with alkyl- on the purine ring system at various ring positions is not a new modification." Id. at 6.

The examiner concludes:

Thus it would have been obvious to one skilled in the art at the time the instant invention was made to expect instant optical isomers in main claim 1 and claims dependent thereon as well as various 2- and/or 6-substituted purines in independent claims 45-48,

55, 63 to be useful against one or more viruses in view of the close structural similarity and equivalency teachings outlined above.
Id.

***4** The panel would like to initially note that review of the issues on appeal was severely hampered by the lack of claim by claim analysis, i.e., the use of a shot-gun rejection. In rejecting claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 over the combination of Holy (US), Webb (EP or US), Yu, Starrett and Karrer, the examiner apparently cites Holy (EP) and Starrett for their teaching of certain derivatives that are only required in the dependent claims. Moreover, the rejection implies that at a minimum, claim 1 is would have been obvious over Holy alone.

Most tellingly, in the response to appellants' argument that Webb cannot be combined with Holy, the examiner responds that

> Webb is not a secondary reference but rather a primary reference applied for showing additional aspects of appellants' invention as obvious, mainly for its teaching of 2,6 diamino phosphonomethoxypropyl purine, but Webb also teaches and claims bases such as 2-amino purine, 8-substituted guanines (guanine per se is excluded in the instant claims) which are within at least claim 1.

Examiner's Answer, page 9.

If Webb was not to be combined with Holy (US), it should have been separately applied, or at least the examiner should have explicitly stated that Webb was being applied in the alternative. The way in which the rejection was laid out, however, makes it difficult to understand, much less rebut and review.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). In order to make a prima facie case of obviousness based on the structural similarity, in this case similarity between the claimed optical isomer and its racemate taught by the prior art, not only must the structural similarity exist, but the prior art must also provide reason or motivation to make the claimed compound. See In re Dillon, 919 F. 2d 688, 692,16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), In re Mayne, 104 F. 3d 1339, 1341, 41 USPQ2d 1451, 1454 (Fed. Cir. 1997); In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 256 (CCPA 1979). Moreover, the prior art has to enable the ordinary artisan to make the claimed compound. See Payne, 606 F.2d at 314. The rejection over Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer does not meet this criteria and thus fails to set forth a prima facie of obviousness.

In the rejection above, the examiner states with respect to the separation of the racemates of Holy (US) that "it is very well known considerably prior to applicants' effective filing to consider the separation of biologically active racemates in order to determine if one is largely responsible for the desired activity," see Examiner's Answer, page 5, but does not set forth any facts or findings to support the motivational statement, especially since all that is currently being claimed is a single isomer, i.e., the R isomer. See In re Lee, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (in reviewing an obviousness rejection, the court noted that "conclusory statements" as to teaching, suggestion or motivation to arrive at the claimed invention "do not adequately address the issue").

***5** With respect to the additional references cited by the examiner for teaching the various other substituents required by the claims, the only motivation that the examiner provides for making the combination is structural similarity. As noted above, however,

structural similarity is not enough, but there must also be some teaching, suggestion, or motivation provided in the prior art to make the combination.

Moreover, appellants also argue that the art teaches away from isolating PMPA or PMPDAP from its isomer. Appellants cite Holy (1989) and DeClercq for teaching that PMPA is an inactive product. See Appeal Brief, pages 19-23. The examiner did not find the teaching away references to be persuasive because Holy filed and obtained a patent for PMPA and other compounds on the basis that the compounds are antiviral.

Obviousness is determined in view of the sum of all of the relevant teachings in the art, not isolated teachings in the art. See In re Kuderna, 426 F.2d 385, 389, 165 USPQ 575, 578 (CCPA 1970); see also In re Shuman, 361 F.2d 1008, 1012, 150 USPQ 54, 57 (CCPA 1966). In assessing the teachings of the prior art references, the examiner should also consider those disclosures that may teach away from the invention. See In re Geisler, 116 F.3d 1465, 1469, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997).

DeClercq states that PMPA is an "inactive product[]". DeClercq, page 264. The examiner dismisses that teaching by arguing that, in context, it appears that DeClercq is referring to the S-isomer. See Examiner's Answer, page 7. When a particular isomer is being referred to by the reference, however, DeClercq seems to indicate as such. Holy (1989) indicates that the replacement of the primary hydroxy group in HPMPA by a methyl group resulted in the loss of activity. See Holy (1989), pages 56-57. Thus, both DeClercq and Holy (1989) teach away from resolving a racemic mixture of PMPA into the currently claimed enantiomer.

In finding that the above prior art references do not teach away from separating a racemic mixture of PMPA into its optically pure isomers, the examiner relies on the Holy (US) patent, apparently bothered by the fact that Holy, who is also an inventor on the instant application, obtained a patent whose claims encompass PMPA. The examiner additionally asserts in support of the rejection that the patent was obtained because the compounds were shown to have antiviral activity.

While PMPA may be encompassed by the group of structures claimed in the Holy (US) patent, that is not dispositive of the issue of whether PMPA has antiviral activity. A claim may encompass inoperative embodiments and still meet the enablement requirement of 35 U.S.C. § 112, first paragraph. See Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984), In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976).

*6 In Table 1 of the Holy (US) patent, specifically referred to by the examiner in rejecting the claims at issue, see Examiner's Answer, page 4, certain chemical characteristics are given for compound 2, i.e., PMPA, but the table does not set forth any biological data. The disclosure of Holy relied upon by the examiner as stating that PMPA has biological activity, i.e., column 4, lines 14-19 of the Holy (US) patent, also does not support the examiner's position. That portion of the patent states:

> Some compounds of the general formula I which are the subject of this invention, are important active components of antiviral drugs. An example of such compound is 9-phosphonylmethoxyethyladenine which exhibits a specific activity against DNA-viruses and Maloney sarcoma (PV 3018-85).

(Emphasis added). Thus, the patent does not assert that all of the compounds have antiviral activity, but that some of the compounds may have antiviral activity. When the disclosure of Holy (US) is read in conjunction with the teachings of DeClercq and Holy (1989), which specifically address PMPA, teaching that compounds such as PMPA do not have antiviral activity, the prior art, when read as a whole, teaches away from

separating a racemic mixture of PMPA into its optically pure isomers.

In addition, the examiner also relies upon Adamson and Eli Lilly as apparently standing for the proposition that an optically pure form of a compound is per se obvious over a disclosure of a racemic mixture of the compound. See Examiner's Answer, page 8 ("The motivation to resolve the racemate of Holy is fully supported by the case law previously cited dealing with racemates vs. individual optical isomers."). One cannot rely on case law alone, however, to provide the motivation to modify a prior art compound. "[T]he question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." In re Rouffet, 149 F.3d 1350, 1356, 47 USPQ2d 1453, 1456 (Fed. Cir. 1998) (citations omitted). In this case, the prior art as a whole, as discussed above, teaches away from making the modification as suggested by the examiner.

Claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 stand provisionally rejected over the claims of co-pending Application No. 07/925,610. As appellants do not present any arguments as to why the rejection is improper, but instead note their intent to file a terminal disclaimer once the copending case is sent to issue, this rejection is affirmed.

CONCLUSION

The rejection of claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 over the combination of Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer is reversed. For the same reasons, the obviousness-type double patenting rejections over the '716 patent and the ' 510 patent as combined with Yu (EP or US), Holy (EP), Starrett and Karrer, and the rejection of claims 12-19 over the combination of Holy (EP), Webb (EP or US), Vemishetti, Alexander, Yu (US or EP) and the Merck Index, are also reversed. Finally, the provisional rejection of claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 over the claims of co-pending application No. 07/925,610 is affirmed.

*7 No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART; REVERSED-IN-PART

BOARD OF PATENT APPEALS AND INTERFERENCES

SHERMAN D. WINTERS

Administrative Patent Judge

ERIC GRIMES

Administrative Patent Judge

LORA M. GREEN

Administrative Patent Judge

FN1. According to the Examiner's Answer, claims 49-54, 56-62, 64 and 79 are free of the prior art, with Claim 79 being objected to, and thus these claims are not subject to the instant appeal. See Examiner's Answer, page 2.

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